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Cationic rhodium(I)/PPh$_3$ complex-catalyzed dehydrogenation of alkanethiols to disulfides under inert atmosphere

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Abstract—A cationic rhodium(I)/PPh$_3$ complex is an effective catalyst for dehydrogenation of primary or secondary alkanethiols to symmetrical disulfides under inert atmosphere. The dependence of reactivity on the structure of thiols is examined in detail.

Selective oxidative coupling of thiols to disulfides is of interest from the viewpoint of both biological and chemical processes.[1] Thiols are among functional groups, which can be easily over-oxidized and, therefore, extensive methods have been reported for their controlled oxidation.[2–6] Most of the existing methods involve the use of a stoichiometric amount of oxidants (e.g. metal oxidants,[2] peroxides,[3] halogens,[4] and air[5]) and suffer from effluence, flammability, explosion, or undesirable side reactions due to their reagents.

Selective metal-catalyzed dehydrogenation of thiols to disulfides under inert atmosphere is a possible alternative to avoid the use of oxidants. Ogawa et al. reported that diphenyl disulfide was formed as a by-product in the reaction of benzenethiol and 1-octyne using a catalytic amount of RhCl(PPh$_3$)$_3$.[6] However, transition metal complex-catalyzed dehydrogenation of thiols to disulfides remains unexplored. The present study describes cationic rhodium(I)/PPh$_3$ complex-catalyzed dehydrogenation of alkanethiols to disulfides under inert atmosphere (Eq. 1).

$$\mathrm{RSH}\ \xrightarrow[\substack{\mathrm{CH_2Cl_2},\ 4\,^{\circ}\mathrm{C},\ 1\,\mathrm{h} \\ \text{under Ar},\ -\mathrm{H_2}}]{\substack{\text{catalytic} \\ [\mathrm{Rh(cod)_2}]\mathrm{BF_4}/8\ \mathrm{PPh_3}}}\ \mathrm{(RS)_2} \qquad (1)$$

We first examined various rhodium catalysts to facilitate this transformation and determined that a cationic rhodium(I)/PPh$_3$ complex showed the highest catalytic activity.[7] The rhodium-catalyzed dehydrogenation of various thiols was investigated in detail as shown in Table 1.[8] The reaction of a primary alkanethiol is highly dependent on reaction temperature and reaction time. The highest yield of disulfides was obtained at 4 °C for 1 h (entry 1). Interestingly, longer reaction time (16 h) at 4 °C decreased the yield of disulfides (entry 2). Furthermore, when the reactions were conducted at 4 °C for 1 h followed by 25 °C for 15 h or at 4 °C for 16 h followed by 25 °C for 24 h, the yield of disulfides decreased further and thiols were regenerated (entries 3 and 4).[9] These results indicate that this dehydrogenation reaction may be reversible and the formation of disulfide is a kinetically favorable process.[10] The reaction of a secondary alkanethiol is also dependent on reaction temperature and reaction time (entries 7–10). The highest yield of disulfides was obtained at 4 °C for 1 h (entry 7). Highly functionalized alkanethiols are also suitable substrates to furnish the corresponding disulfides in good yield (entries 5 and 6). However, tertiary alkanethiol **1e** or arenethiol **1f** is not a suitable substrate, furnishing disulfide in very low yield or not at all (entries 11 and 12).

The dependence of reactivity on the structure of thiols suggested to us that we might be able to effect selective dehydrogenation of two structurally different thiols to disulfides (Eq. 2). Treatment of a mixture of primary alkanethiol **1a** and tertiary alkanethiol **1e** predominantly furnished primary alkyl disulfide **2a**, and disulfide **3** or **2e** was obtained in low yield or not at all. Interestingly,

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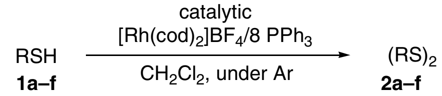
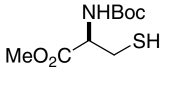
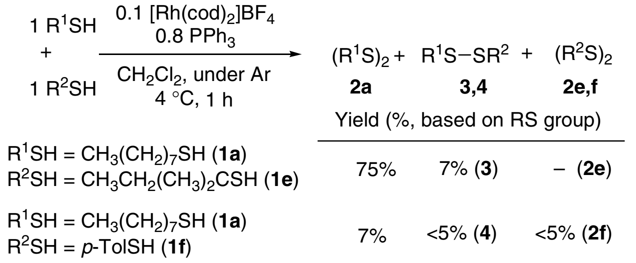
Table 1. Cationic rhodium(I)/PPh_3 complex-catalyzed dehydrogenation of thiols[a]



Entry	RSH	Rh (%)	Temperature (°C)	Time (h)	$(RS)_2$	Yield (%)[b]
1	$CH_3(CH_2)_7SH$ (**1a**)	5	4	1	(**2a**)	**86**
2		5	4	16		78
3[c]		5	4→25	1+15		66[e] (24[e,f])
4[d]		5	4→25	16+24		30[e] (52[e,f])
5	$HO(CH_2)_{11}SH$ (**1b**)	10	4	1	(**2b**)	**78**
6	 (**1c**)	10	4	1	(**2c**)	**72**
7	CySH (**1d**)	5	4	1	(**2d**)	**87**
8		5	4	16		80
9[c]		5	4→25	1+15		75[e]
10[d]		5	4→25	16+24		67[e]
11	$CH_3CH_2C(CH_3)_2SH$ (**1e**)	5	4	16	(**2e**)	—
12	*p*-TolSH (**1f**)	5	4	16	(**2f**)	**<5[e]**

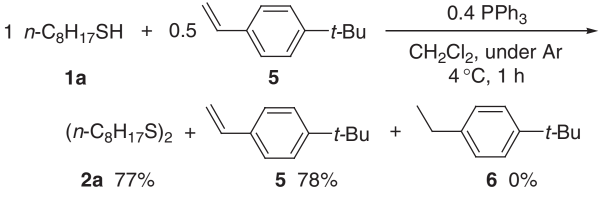
[a] The reaction was conducted using RSH (0.5 mmol), $[Rh(cod)_2]BF_4$ (0.025 or 0.05 mmol), PPh_3 (0.2 or 0.4 mmol), and CH_2Cl_2 (2 mL).
[b] Isolated yield.
[c] The reaction was conducted at 4 °C for 1 h, then at 25 °C for 15 h.
[d] The reaction was conducted at 4 °C for 16 h, then at 25 °C for 24 h.
[e] Determined by ^1H NMR using hexamethylbenzene as an internal standard.
[f] Recovery of RSH.

the presence of arenethiol **1f** significantly lowered the yield of primary alkyl disulfide **2a**.



(2)

Because the cationic rhodium(I) complexes are effective catalysts for the hydrogenation of olefins, the tolerance of olefins in the dehydrogenation of thiols is of interest. Dehydrogenation of **1a** conducted in the presence of 4-*t*-butylstyrene (**5**) furnished disulfide **2a** in 77% yield and 4-*t*-butylethylbenzene (**6**) was not detected at all (Eq. 3). This result strongly contrasts with the oxidative amination of styrene, which furnished ethylbenzene in high yield.[11]



(3)

In conclusion, we have determined that a cationic rhodium(I)/PPh_3 complex is an effective catalyst for dehydrogenation of primary or secondary alkanethiols to symmetrical disulfides under inert atmosphere. Future work will include additional studies of the scope and mechanism of this transformation, and the utilization of this transformation to a variety of organosulfur chemistry processes.

Acknowledgements

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7. The use of other phosphine ligands (e.g. *n*-Bu_3P, Cy_3P, dppe), different amounts of PPh_3, neutral rhodium(I) complexes, or cationic iridium(I) complexes significantly lowered the yield of disulfides.
8. Sample procedure (Table 1, entry 1): Under Ar atmosphere, PPh_3 (52.5 mg, 0.20 mmol) and $[Rh(cod)_2]BF_4$ (10.2 mg, 0.025 mmol) were dissolved in CH_2Cl_2 (1.0 mL) and the mixture was stirred for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring for 0.5 h at room temperature, the resulting solution was concentrated to dryness. The residue was dissolved in CH_2Cl_2 (1.0 mL) and transferred to CH_2Cl_2 (1.0 mL) solution of octanethiol (**1a**) (73.1 mg, 0.50 mmol) in a 30-mL screw-cap vial at room temperature. The mixture was kept at 4 °C for 1 h under Ar atmosphere. The resulting solution was concentrated and purified by preparative TLC (hexane), which furnished dioctyl disulfide (**2a**) (62.4 mg, 0.21 mmol, 86%).
9. When dioctyl disulfide (**2a**) was treated with H_2 in the presence of $[Rh(cod)_2]BF_4/8\ PPh_3$ (5%, based on RS group) for 5 h, octanethiol (**1a**) was generated in 7% yield.
10. The reaction conducted in a screw-cap vial at 4 °C gave a higher yield of disulfide and higher reaction rate than the reaction conducted under reduced pressure ($\sim$5 mmHg) at room temperature.
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